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(71) Applicant (*for all designated States except US*): THE GOVERNMENT OF THE UNITED STATES OF AMERICA, represented by THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES The National Institutes of Health [US/US]; Office of Technology Transfer, 6011 Executive Boulevard Suite 325, Rockville, MD 20852 (US).

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

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Exhibit C

(54) Title: UTEROGLOBIN IN THE TREATMENT OF IgA MEDIATED AUTOIMMUNE DISORDERS

(57) Abstract: Uteroglobin has been discovered to prevent IgA mediated diseases, such as IgA nephropathy, by preventing the deposition of IgA-Fibronectin immunocomplexes in tissues such as the renal glomeruli. The invention therefore includes methods of treating such diseases by administering therapeutically effective amounts of uteroglobin (and variants or mimetics) to prevent or im-

## INTERNATIONAL SEARCH REPORT

Int'l. Application No  
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A. CLASSIFICATION OF SUBJECT MATTER  
 IPC 7 A61K38/17 G01N33/50 G01N33/68 C12Q1/68 A61P31/12  
 A61P29/00 A61P11/00 //A01K67/00, C07K14/47, C12N15/12,  
 (A61K38/17, 31:56)

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
 IPC 7 A61K A01K C07K C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, BIOSIS, MEDLINE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 53846 A (CLARAGEN INC ; NAT INST HEALTH (US)) 3 December 1998 (1998-12-03)	1, 2, 4-9, 11, 12, 16-23, 36-46
A	the whole document ---	9-15
A	DEMAYO F J: "Advantages and pitfalls of transgenic and mutant animals" AMERICAN JOURNAL OF KIDNEY DISEASE, vol. 33, no. 3, March 1999 (1999-03), pages 598-600, XP000961156 the whole document ---	-/--

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

## \* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

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19 March 2001

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## INTERNATIONAL SEARCH REPORT

Inte	onal Application No
PCT/US 00/09979	

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	NORTIER J ET AL: "Proximal tubular injury in Chinese herbs nephropathy: Monitoring by neutral endopeptidase enzymuria." KIDNEY INTERNATIONAL, vol. 51, no. 1, 1997, pages 288-293, XP000691142 the whole document ---	27, 29
P, X	ZHENG F ET AL: "Uteroglobin is essential in preventing immunoglobulin A nephropathy in mice." NATURE MEDICINE, vol. 5, no. 9, September 1999 (1999-09), pages 1018-1025, XP002154608 the whole document ---	1-29
X	LAING I A ET AL.: "A polymorphism of the CC16 gene is associated with an increased risk of asthma" JOURNAL OF MEDICAL GENETICS, vol. 35, no. 6, June 1998 (1998-06), pages 463-467, XP000971093 the whole document ---	30, 31, 33
T	SZELESTEI T ET AL: "Association of a uteroglobin polymorphism with rate of progression in patients with IgA nephropathy" AMERICAN JOURNAL OF KIDNEY DISEASE, vol. 36, no. 3, September 2000 (2000-09), pages 468-473, XP000961153 the whole document ---	30, 32, 33
A	MATHIS A ET AL.: "Isolates of Encephalitozoon cuniculi from farmed blue foxes (Alopex lagopus) from Norway differ from isolates from Swiss domestic rabbits (Oryctolagus cuniculus)" PARASITOLOGY RESEARCH, vol. 82, no. 8, 1996, pages 727-730, XP000990209 the whole document ---	30, 34
A	HILDEBRANDT F & VOLLMER M: "Familial fibrillary glomerulopathies: What is the role of fibronectin?" ADVANCES IN NEPHROLOGY, vol. 28, 1998, pages 429-437, XP000961154 page 435 -page 436 -----	

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 00/09979

### Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
  
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Although claims 1-9, 18-23, 36-38 are directed to methods of treatment of the human body, the search has been carried out and based on the alleged effects of the composition.

It was assumed that claim 12 refers to claim 9 and that claim 46 refers to claim 39; these being obvious errors. It was envisioned that claim 36 might actually refer to claim 30, the context of claim 36 being ambiguous, but the litteral reading of claim 36 was held: claim 36 refers to claim 1.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: all claims (30-35 partially)

1.1. Claims: 1-29, 36-46

Treatment and diagnosis of IgA mediated autoimmune diseases using uteroglobin. Screening for agents that prevents IgA mediated autoimmune disorders. Treatment of pulmonary inflammation. Uteroglobin composition.

1.2. Claims: 30-35 partially

Genetic diagnosis of predisposition to asthma and IgA mediated autoimmune disorders by screening for A38G polymorphism in the uteroglobin gene.

2. Claims: 30-35 partially

Genetic diagnosis of predisposition to asthma and IgA mediated autoimmune disorders by screening for GTTT repeats polymorphism in the uteroglobin gene.

Please note that all inventions mentioned under item 1, although not necessarily linked by a common inventive concept, could be searched without effort justifying an additional fee.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/09979

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9853846	A 03-12-1998	AU	7707498 A	30-12-1998
		CN	1281367 T	24-01-2001
		EP	1023081 A	02-08-2000